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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/692,401	10/19/00	HEIDECKER L	L0461/7097-(

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EXAMINER	
DIBRINO, M	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 07/03/01

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/692,401	Heldecker et al.
Examiner	**Art Unit**
Marianne DiBrino	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Mar 29, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-4, 7, 8, 10, 16, 18-20, 34, 40-44, 46, 52, and 53 is/are pending in the application.

4a) Of the above, claim(s) 10, 16, 18-20, 34, 40, 41, 44, 46, 52, and 53 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-4, 7, 8, 42, and 43 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9 3/24/01

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment filed 3/29/01 is acknowledged and has been entered.

Claims 1-4, 7, 8, 10, 16, 18-20, 34, 40-44, 46, 52 and 53 are pending.

2. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-4, 7, 8, 42 and 43, drawn to an MAGE-A12 HLA class I-binding peptide/functional variant thereof, and composition and thereof, classified in Class 530, subclass 328.

II. Claims 16 and 18, drawn to a method for enriching for T cells specific for MAGE-A12 HLA class I-binding peptides, classified in Class 435, subclass 325.

III. Claims 19 and 20, drawn to a method for diagnosing a disorder, classified in Class 435, subclass 7.2.

IV. Claim 34, drawn to a polypeptide that binds the peptide of claim 1, classified in Class 530, subclasses 387.1 and 388.1.

V. Claims 40, 41 and 44, drawn to an APC and vaccine composition thereof, classified in Class 424, subclass 93.7.

VI. Claims 52 and 53, drawn to a protein microarray, classified in Class 530, subclass 402.

3. Inventions II and III are different methods.

These inventions require different ingredients and process steps to accomplish enriching T cells (Invention II) or diagnosing a disorder (Invention III). For example, the method of Invention II contacts a sample containing T cells specific for a MAGE-A12 peptide with a complex of HLA class I/peptide, whereas the method of Invention III contacts a biological sample from a subject with an agent, such as for example a CTL or an antibody, which is specific for a MAGE-A12 class I-binding peptide.

Therefore they are patentably distinct.

4. Inventions I, IV, V and VI are different products.

An HLA class I binding peptide (Invention I) is different from a polypeptide that binds to an HLA class I binding peptide (Invention IV) because the class I binding peptide is from 9-11 amino acid residues in length and binds to a class I molecule, whereas the polypeptide of Invention IV, which can be an antibody or antigen-binding fragment thereof, is a larger polypeptide or protein with a different structure, sequence and function, i.e., it binds to the class I binding peptide of Invention I. Both are different from an APC because an APC is a cell which comprises proteins, lipids, carbohydrates among other substances. All are different from a protein microarray because a protein microarray is a solid support structure which comprises an array of peptides of defined sequence.

Therefore they are patentably distinct.

5. Inventions IV and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)).

In the instant case, the product as claimed can be used in a materially different process such as immunopurification procedures or alternatively as an antigen for the production of antibodies.

6. Because these inventions are distinct for the reasons given above and the search required for any group from Group I-VI is not required for any other group from Groups I-VI and Groups I-VI have acquired a separate status in the art as shown by their different classification and divergent subject matter, restriction for examination purposes as indicated is proper.

7. **If Applicant elects Invention I**, Applicant is further required to (1) elect a single disclosed species of peptide/variant/composition thereof (a ***specific SEQ ID NO***, for example, SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

8. **If Applicant elects Invention II**, Applicant is further required to (1) elect a specific agent presenting a complex comprising a specific peptide to be used in the said method (a ***specific SEQ ID NO***, for example,SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

9. **If Applicant elects Invention III**, Applicant is further required to (1) elect a specific agent that is specific for a specific peptide to be used in the said method (a ***specific SEQ ID NO***, for example, SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

10. **If Applicant elects Invention IV**, Applicant is further required to (1) elect a specific polypeptide that binds a specific peptide (a ***specific SEQ ID NO***, for example,SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

11. **If Applicant elects Invention V**, Applicant is further required to (1) elect a specific APC/vaccine composition thereof, that presents a complex comprising a specific peptide (a ***specific SEQ ID NO***, for example,SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

12. **If Applicant elects Invention VI**, Applicant is further required to (1) elect a specific protein microarray that comprising a specific peptide (a ***specific SEQ ID NO***, for example,SEQ ID NO: 6) to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

These species are distinct because their structures are different.

13. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

14. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

15. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species.

M.P.E.P. § 809.02(a).

16. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

17. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

18. During a telephone conversation with Mr. John Van Amsterdam on 6/18/01, a provisional election was made to prosecute the invention of Group I, claims 1-4, 7, 8, 42 and 43 and to select the species, SEQ ID NO: 6. Affirmation of this election must be made by applicant in responding to this Office action.

19. Accordingly, claims 10, 16, 18-20, 34, 40, 41, 44, 46, 52 and 53 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Upon consideration of the prior art, the search has been extended to include SEQ ID NO: 5.

Claims 1-4, 7, 8, 42 and 43 are presently being examined.

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

22. Claims 1-4, 7, 8, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed inven-

written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed isolated MAGE-A12 peptide/composition, including vaccine composition thereof comprising the amino acid sequence of SEQ ID NO: 4, 5 or 6 or a functional variant thereof, fragments thereof which bind HLA class I molecules, or of the said peptide comprising a fragment of the amino acid sequence of SEQ ID NO: 2 which binds HLA-Cw*07, or functional variant thereof.

The instant claims encompass a peptide comprising SEQ ID NO: 4, 5 or 6/variants or fragments thereof, or comprising a fragment of the amino acid sequence of SEQ ID NO: 2 which binds HLA-Cw*07/functional fragment thereof, and compositions or vaccine compositions thereof. The said peptide/variants/fragments and vaccine thereof can comprise amino acid residues that flank the said sequences in the protein of origin, or can be any number of undisclosed and unrelated sequences, and can comprise any peptide with at least one amino acid residue in common with SEQ ID NO: 4, 5 or 6 which binds to any class I HLA molecule. There is insufficient disclosure in the specification on the said peptides/fragments/variants and compositions thereof.

The specification discloses that the human MAGE-A12 gene (SEQ ID NO: 1) encodes a tumor rejection antigen presented by HLA-Cw*07 (the sentence spanning pages 3 and 4). The specification further discloses that peptides derived from the MAGE-A12 polypeptide (SEQ ID NO: 2), when presented by an antigen presenting cell having an HLA class I molecule, effectively induce the activation and proliferation of CD8+ CTL (page 4 at lines 1-4). The specification discloses an octamer, nonamer and decamer peptide, SEQ ID NO: 6, 4 and 5, respectively, and an additional nonamer peptide, SEQ ID NO: 3. The specification discloses that "the isolated MAGE-A12 HLA class I binding peptide preferably is not the full length MAGE-A12 polypeptide sequence" (page 4 at lines 13-15). The specification also discloses that the functional variant includes one or more amino acid additions, substitutions or deletions (page 4 at lines 7-8), and further that "functional variant or variant of a MAGE-A12 HLA binding peptide is a molecule which contains one or more modifications to the primary amino acid sequence of the MAGE-A12 HLA binding peptide and retains the HLA class I binding properties...as well as the ability to stimulate proliferation and/or activation of CD8+ lymphocytes."

The specification does not disclose longer peptides that comprise SEQ ID NO: 3, 4, 5, or 6 (page 4 at lines 11-21). The specification does not disclose fragments of these SEQ ID NO that bind HLA-Cw*07, other than SEQ ID NO: 6 which is a fragment of SEQ ID NO: 4 and 5, and SEQ ID NO: 4 which is a fragment of SEQ

ID NO: 5. The specification does not disclose functional variants or variants of SEQ ID NO: 3, 4, 5, or 6. The specification does not disclose fragments of the amino acid sequence of SEQ ID NO: 2 which bind to HLA-Cw*07, or functional fragments thereof, other than the aforementioned SEQ ID NO. The specification does not disclose isolated MAGE-A12 peptides that bind to HLA class I molecules other than HLA-Cw*07.

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "an isolated MAGE-A12 HLA class I binding peptide comprising the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof which binds HLA class I molecules" or the said peptide wherein the peptide consists of fragments of SEQ ID NO: 4, 5 or 6 or functional variants thereof or the said peptide "comprising a fragment of the amino acid sequence of SEQ ID NO: 2 that binds HLA Cw*07, or a functional variant thereof", is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of containing a portion of SEQ ID NO: 2, 4, 5 or 6, and which may or may not have flanking sequences that are not found in SEQ ID NO: 2. It does not specifically define any of the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they comprise portions of SEQ ID NO: 2, 4, 5 or 6. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. In addition, a definition by a functional property does not suffice to define the genus because it is only an indication of what the property the peptide has, and if one extends the analysis in the instant case, what the peptide does (i.e., it binds to an HLA class I molecule or to HLA-Cw*07), rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

There is no disclosure of a genus of peptides comprising SEQ ID NO: 4, 5 or 6, fragments thereof or variants thereof, or of peptides comprising a fragment of the

amino acid sequence of SEQ ID NO: 2 which binds HLA Cw*07 or a functional variant thereof. One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

23. Claims 1-4, 7, 8, 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated MAGE-A12 HLA class I binding peptide consisting of SEQ ID NO: 4, 5 or 6 does not reasonably provide enablement for making and/or using the claimed isolated MAGE-A12 HLA class I binding peptide: (1) which is a functional variant of SEQ ID NO: 6, nor (2) which is a functional variant or fragment of SEQ ID NO: 4 or 5, (3) a composition, including a vaccine composition, comprising any of (1) or (2), other than SEQ ID NO: 6 which is a fragment of SEQ ID NO: 4 and 5, and SEQ ID NO: 4 which is a fragment of SEQ ID NO: 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification does not disclose how to make and use the said claimed isolated MAGE-A12 HLA class I binding peptide functional variant or fragment. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass peptides which have one or more amino acid additions, substitutions or deletions and/or which comprise flanking sequences that are undisclosed and unrelated to SEQ ID NO: 2.

The specification discloses that the human MAGE-A12 gene (SEQ ID NO: 1) encodes a tumor rejection antigen presented by HLA-Cw*07 (the sentence spanning pages 3 and 4). The specification further discloses that peptides derived from the MAGE-A12 polypeptide (SEQ ID NO: 2), when presented by an antigen presenting cell having an HLA class I molecule, effectively induce the activation and proliferation of CD8+ CTL (page 4 at lines 1-4). The specification discloses an octamer, nonamer and decamer peptide, SEQ ID NO: 6, 4 and 5, respectively, and an additional nonamer peptide, SEQ ID NO: 3. The specification discloses that "the isolated MAGE-A12 HLA class I binding peptide preferably is not the full length MAGE-A12 polypeptide sequence" (page 4 at lines 13-15). The specification also discloses that the functional variant includes one or more amino acid additions, substitutions or deletions (page 4 at lines 7-8), and further that "functional variant or variant of a MAGE-A12 HLA binding peptide is a molecule which contains one or more modifications to the primary amino acid sequence of the MAGE-A12 HLA binding peptide and retains the HLA class I binding properties...as well as the ability to stimulate proliferation and/or activation of CD8+ lymphocytes." The specification also discloses that sequence motifs for MAGE-12 HLA binding peptide functional variants can be developed by analysis of the binding pockets of MHC HLC-Cw proteins and/or the TCR contact points of the

MAGE-A12 immunogenic polypeptides disclosed in the instant application (page 13 at lines 10-13). The specification discloses that classes of peptides can be identified which have a likelihood of binding to a particular HLA molecule and of interacting with a TCR, the said peptides can be synthesized and tested for activity, i.e., induction of a T cell response (page 13 at lines 17-22).

For purposes of examination, the instant claims are given their broadest reasonable interpretation. Therefore, the variant or fragment can be any length. Such additional amino acid residues, or lack of a sufficient number of amino acid residues, could prevent complex formation between said peptides and the HLA molecules. For instance, the length of the peptide is important for binding to HLA (along with the presence of anchor (or "motif") amino acid residues present within the peptide). The peptides that bind to class I molecules have a predominant length. A primary factor for this is that amino acid residues at the amino- and carboxy-termini of peptides binding to class I molecules interact with conserved amino acid residues in pockets ("a","F") located at opposite ends of the binding groove of the class I molecule, giving rise to a common orientation of the peptides in the binding site (Engelhard at page 14, column 1, lines 16-27, of record.) Thus, the amino acid residues at the peptides' termini make a network of hydrogen bonds with conserved residues on the sides and bottom of the peptide-binding groove of class I molecules. These interactions are important for holding the peptides in the binding groove and for stabilizing the complex (Guo, et al at page 366, column 1 lines 1-10, of record.) "...the preferred length (of the peptide) is determined by the minimum amount of peptide required to span the center of the binding site and optimize the interactions at the ends." (Engelhard at page 14, column 1, lines 23-27.) The minimum amount of peptide required to span the binding groove and make favorable contacts with their N-and C-termini may be dependent upon the sequence of the peptide itself since different amino acid residues have different physicochemical properties, and may be dependent upon the identity of the additional amino acids, since these residues may make a negative contribution to binding. Accordingly, there is a high level of unpredictability in excising immunogenic peptides from longer sequences, or of providing longer sequences themselves, or for providing sequences shorter than 9-10 amino acid residues in length that would still maintain binding function, and Applicant does not provide direction or guidance to do so.

There is no guidance in the specification as to what alterations result in a functional variant or fragment. Because of this lack of guidance, the extended experimentation that would be required to determine which additions, deletions or substitutions would be acceptable to retain functional activity, especially as the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are therefore not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, Merz & LeGrand, Birkhauser Boston, pages 491-495, 1994, entire article, especially Section 6,

paragraph 1, of record), it would require undue experimentation for one of skill in the art to arrive at other amino acid sequences that would have functional activity. In other words, since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make and use the corresponding sequences. The enablement provided by the specification is not commensurate with the scope of the claims. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

24. The following is a quotation of the second paragraph of 35 U.S.C.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

25. Claims 1-3, 7, 42 and 43 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 is indefinite in the recitation of "HLA class I molecules" because "molecules" should be recited in the singular "molecule".

b. Claims 2 and 3 are indefinite in the recitation of "fragments" and "variants" because the said limitations should be recited in the singlular "fragment" and "variant".

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 1-4, 7, 8, 42 and 43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over PIR_68 Accession No. I54519 (1996) in view of U.S. Patent No. 5,846,827, U.S. Patent No. 5,662,907 and Rammensee et al (Immunogenetics, 41: 178-228, 1995) and admissions in the specification (Figure 4 and Brief Description of the Drawings for Figure 4).

PIR_68 Accession No. I54519 teaches that VVRIGHLYIL is amino acid residues 169-178 of MAGE-A12 protein, which is a MAGE-1 related gene, and teaches the MAGE-A12 protein sequence. VVRIGHLYIL is SEQ ID NO: 5 of the instant application.

PIR_68 Accession No. I54519 does not teach an isolated peptide with the sequence VVRIGHLYIL, nor a composition thereof, including a vaccine composition comprising an adjuvant and a pharmaceutical carrier, nor a composition thereof comprising another class I or class II HLA binding peptide not from MAGE- A12 protein.

U.S. Patent No. 5,846,827 discloses that definition of motifs specific for different class I alleles allows the identification of potential peptide epitopes from an antigenic protein whose amino acid sequence is known (especially the sentence spanning columns 4 and 5) and synthesis of the peptides (especially column 5 at lines 1-4). U.S. Patent No. 5,846,827 discloses that potential antigenic target proteins include melanoma antigens such as MAGE-1 (especially column 4 at lines 38-48). U.S. Patent No. 5,846,827 further discloses that the peptides will be of 9 or 10 amino acid residues in length (especially column 5 at lines 63-67). U.S. Patent No. 5,846,827 also discloses HLA-A2 (especially Example 2 and Example 3).

U.S. Patent No. 5,662,907 discloses a pharmaceutical composition comprising a class I HLA binding peptide from MAGE-3 tumor antigen precursor protein, EVDPIGHLY, which further comprises a pharmaceutically acceptable carrier and when used as a vaccine, further comprises an adjuvant (especially column 2 "Summary of the Invention"). U.S. Patent No. 5,662,907 further discloses linking the class I HLA binding peptide with another peptide such as a Th epitope peptide, i.e., an HLA-class II binding peptide, that is not from MAGE-A12 (especially column 5 at lines 14-18 and column 7 at lines 63-67 and column 8).

Rammensee et al teach the anchor residue motif for peptides that bind to HLA-A2 include Val ("V") at position 2 of the peptides and Leu ("L") at the carboxy terminus of the peptides (especially Table 2 on page 194).

The admission in the instant specification on page 4 at lines 16-21 is that SEQ ID NO: 5 of the instant application binds to HLA Cw*07 and is a fragment of Seq ID NO: 2 of the instant application.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have scanned the MAGE-A12 protein sequence taught by PIR_68 Accession No. I54519 using the motif of position 2 Val and a carboxy terminal Leu taught by Rammensee et al for peptides that bind to HLA-A2 for a decamer subsequence corresponding

to amino acid residues 169-178, i.e., VVRIGHLYIL, of MAGE-A12, as per the disclosure of U.S. Patent No. 5,846,827 that definition of motifs specific for different class I alleles allows the identification of potential peptide epitopes from an antigenic protein whose amino acid sequence is known, and to have synthesized the said subsequence as disclosed by U.S. Patent No. 5,846,827 for inclusion in a pharmaceutical or vaccine composition comprising a pharmaceutically acceptable carrier and further comprising an adjuvant or another HLA binding peptide as disclosed by U.S. Patent No. 5,662,907 for class I binding peptides from another antigenic protein MAGE-3.

One of ordinary skill in the art would have been motivated to do this in order to treat melanomas or other tumors expressing the MAGE-1 related protein MAGE-A12 taught by PIR_68 Accession No. I54519 in HLA-A2 positive individuals because U.S. Patent No. 5,846,827 discloses that potential antigenic target proteins from which to identify potential class I HLA binding peptide epitopes, including those that bind to HLA-A2, include melanoma antigens such as MAGE-1 and U.S. Patent No. 5,662,907 discloses a pharmaceutical composition comprising a class I HLA binding peptide from another tumor antigen protein which further comprises a pharmaceutically acceptable carrier and when used as a vaccine, further comprises an adjuvant, or which can comprise another HLA binding peptide, and because the motif for peptides that bind to HLA-A2 was known in the art as taught by Rammensee et al.

Instant claim 1 is included in this rejection because the reference peptide VVRIGHLYIL, which is SEQ ID NO: 5 of the instant application comprises the amino acid sequence of RIGHLYIL, SEQ ID NO: 6, of the instant application. Instant claim 4 is included in this rejection because the reference peptide is a fragment of the amino acid sequence of SEQ ID NO: 2 of the instant application and SEQ ID NO: 2 is the protein MAGE-A12. The instant claim 4 is also included in this rejection because the reference peptide binds to HLA Cw*07 and is a fragment of SEQ ID NO: 2 of the instant claim 4 (The specification at lines 16-21).

28. No claim is allowed.

29. SEQ ID NO: 6 appears to be free of the prior art.

30. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application

should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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